

## Research Article

Fumihiko Koyama, Takeshi Yoda\*, Tomohiro Hirao

# Insomnia and depression: Japanese hospital workers questionnaire survey

<https://doi.org/10.1515/med-2017-0056>

received May 23, 2017; accepted October 12, 2017

**Abstract:** Objectives: This study aimed to identify a correlation between insomnia and the occurrence of depression among Japanese hospital employees using the data obtained from a self-reported questionnaire.

**Methods:** A self-administered questionnaire on sleeping patterns, depression, fatigue, lifestyle-related diseases, and chronic pain was given to 7690 employees aged 20-60 years, and 5,083 employees responded.

**Results:** An insomnia score of  $>2$  was observed in 840 (13%) respondents. Chronic insomnia correlated significantly with gender, occupation, overtime work, metabolic syndrome, chronic pain, fatigue, and depression. Moreover, significant negative effects on depression scores were observed in males aged 30-39 (partial regression coefficient:  $b=0.357$ ,  $p=0.016$ ), females aged 20-29 ( $b=0.494$ ,  $p<0.001$ ), male administrative staff ( $b=0.475$ ,  $p=0.003$ ), males with metabolic syndrome ( $b=0.258$ ,  $p=0.023$ ), and both genders with chronic insomnia (male;  $b=0.480$ ,  $p<0.001$ ; female;  $b=0.485$ ,  $p<0.001$ ), and fatigue (male;  $b=1.180$ ,  $p<0.001$ ; female;  $b=1.151$ ,  $p<0.001$ ).

**Discussion:** Insomnia is a risk factor for depression and for other lifestyle-related diseases. The insomnia score may be useful in preventative care settings because it is associated with a wide spectrum of diseases and serves as a valuable marker for early detection of depression. Thus, our future studies will focus on establishing a method for

early detection of depression symptoms among workers across various job profiles.

**Keywords:** Insomnia, depression; Fatigue; Lifestyle-related diseases; Chronic pain; Early detection

## 1 Introduction

The number of yearly suicides in Japan was over 30,000 for 14 consecutive years beginning in 1988, and is highest among middle-aged males, the most productive age group. Suicide has become a leading cause of death, rivaling cancer, neural diseases, and heart diseases. An estimate of the financial impact caused by workers who had to take time off or passed away because of mental illness was reported to be 4.1 billion US dollars annually by UPI world news ([https://www.upi.com/Top\\_News/World\\_News/2017/03/24/Japan-suicides-costing-country-41-billion-annually/1421490375745/](https://www.upi.com/Top_News/World_News/2017/03/24/Japan-suicides-costing-country-41-billion-annually/1421490375745/)). Thus, mental illness, including depression, is an issue that leads to substantial financial losses and a decline in the working population.

The Japan Labor Health and Welfare Organization established Workers' Preventative Health Care Centers (WPHCCs) in nine hospitals for laborers across the country in 2001. The WPHCCs offer preventative measures to combat health disorders caused by overworking, to promote the mental health of workers, and to provide health management resources for working women. As a part of the WPHCC's duties, a research study comprising 13 fields of work-related injuries and illness was conducted in 2004-2008. In the mental health field, Koyama et al. reported that the change of cerebral blood flow using  $^{99m}\text{Tc}$ -ECD SPECT was associated with the phases of depression and remission, degree of accumulated fatigue, subjective fatigue, and sleep disorders [1-3]. Brain function imaging showed that those who scored highly in the Insomnia Score (IS) items of the Structured Interview Guide for the Hamilton Depression Rating Scale (SIGH-D) [4] had a significant decrease in blood flow in their dorsal

---

\*Corresponding author: Takeshi Yoda, Department of Public Health, Faculty of Medicine, Kagawa University, 1750-1, Ikenobe, Miki-cho, Kagawa 761-0793, JAPAN, TEL: +81-(0)87-891-2133, FAX: +81-(0)87-891-2134, E-mail: tyoda@med.kagawa-u.ac.jp

Fumihiko Koyama, Department of Occupational Mental Health with Return to Work Support Services, Toho University Sakura Medical Center, Japan

Tomohiro Hirao, Department of Public Health, Faculty of Medicine, Kagawa University, Japan

frontal lobe [3]. Thus, the imaging shows that a chronic sleeping disorder is closely related to depression.

A preliminary study on the association between the severity of a sleeping disorder and depression was conducted with 108 participants. The results showed that the IS was significantly related to the severity of depression, subjective fatigue, and feeling of hopelessness [3]. Therefore, the IS might be an effective tool for early detection of those at risk of depression and for suicide prevention.

In this study, we conducted a large-scale nationwide survey to examine the relationship between chronic sleep disorders and depression and several health-related parameters. Hospital employees work especially long hours, and this is now big problem not only in Japan but also in some developed countries [5-7]. We therefore conducted this survey in 10 hospitals in Japan.

## 2 Methods

### 2.1 Participants

The participants were between the ages of 20 and 60 years and included staff members (including part-time, temporary, or hourly-wage employees) at 10 Rosai hospitals (Hokkaido, Tohoku, Tokyo, Kanto, Chubu, Osaka, Kansai, Chugoku, Kagawa, and Kyushu) and the staff of the Japan Labor Health and Welfare Organization headquarters. Each participant understood the objectives of this study and consented to participate. The Medical Research Ethics Committee designated by the Japan Labor Health and Welfare Organization on March 31, 2011 approved this study.

### 2.2 Measures

The survey was conducted with a self-administered anonymous questionnaire. The items on the questionnaire included gender, age, and job type (i.e., doctors, nurses, medical care personnel, administrative staff members, and skilled professionals), and the items related to the following four categories.

#### 1. Sleeping history in the last two weeks.

Six items related to early insomnia (initial insomnia), middle insomnia, and late insomnia (terminal insomnia) from the Structured Interview Guide for the Hamilton Depression Rating Scale (SIGH-D) [4], which rates the severity of depression, were administered. Participants

indicated if they had experienced any of the following: 1) There are times where it takes more than 30 min to fall asleep, 2) I have a hard time falling asleep almost every day, 3) Although there are times when I wake up during the night, I can go back to sleep again, 4) I wake up during the night and get out of bed, 5) I wake up earlier than usual in the morning but then go back to sleep, and 6) I often wake up earlier than usual in the morning and I usually stay awake. This scale is very well known for evaluation of depression. It has been translated into Japanese, is also validated for a Japanese version [8] and is widely used for detection of major depression disorders in Japanese patients [9-11].

Positive responses to items 1, 3, and 5 received a score of “1” and positive responses to items 2, 4, and 6 received a score of “2”. The IS was calculated by adding the scores. Koyama *et al.* reported that subjects who suffered from severe sleeping disorders, not just during depression, tended to have decreased blood flow in the frontal lobe using  $^{99m}\text{Tc}$ -ECD SPECT [2]. When SIGH-D was used to evaluate sleeping disorders, an IS of 3 or higher showed that its severity and the decrease in blood flow in the frontal lobe were significantly correlated. In other words, based on our preliminary studies [1-3], the severity of insomnia and the decrease in blood flow in the dorsal frontal lobe were correlated when the IS was  $>2$ , while no significant cerebral blood flow changes were seen when the IS was  $\leq 2$ . Therefore, the IS cutoff value for this current study for determining significant chronic insomnia was set as 3.

#### 2. Overtime work.

Participants rated the amount of overtime work they performed in the past month on a four-point scale: under 20 hours, 20–39 hours, 40–79 hours, and over 80 hours.

#### 3. Lifestyle-related diseases and chronic pain.

The participants indicated a current treatment or health guidance in the following five illnesses: hypertension, diabetes, metabolic syndromes, low back pain, and headaches.

#### 4. Subjective fatigue and depression.

The participants were asked to answer items related to fatigue (three items) and depression (six items) from the brief job stress questionnaire [12] on a four-point scale: “rarely”, “sometimes”, “often”, and “almost always”. The items related to fatigue were: “I am extremely tired”, “I am exhausted”, and “I feel lethargic”. The items related to depression were: “I feel depressed”, “I feel too tired to do anything”, “I cannot concentrate on things”, “I cannot shake off the blues”, “I cannot concentrate on my work”, and “I feel sad”. The scores were summed, and the total

fatigue score (FS) ranged from 3 to 12 points, and the total depression score (DS) ranged from 6 to 24 points.

The questionnaires were sent and collected via the post to the staff members who worked at 11 facilities, including each of 10 Rosai hospitals, and the Japan Labor Health and Welfare Organization's headquarters between June 1 and July 29, 2011. Answered questionnaires were collected at Kagawa Rosai Hospital Work-Related Injuries/Illness Research Center.

## 2.3 Statistical analysis

Based on the preliminary studies [1-3], participants with an IS higher than 3 were considered suffering from chronic insomnia. The relationship between chronic insomnia and age, gender, occupation, overtime work, lifestyle-related diseases, fatigue, and depression was analyzed. A multiple regression analysis setting the DS as an objective variable was conducted to investigate the effect of chronic insomnia on depression. The Chi-square test was used to compare group differences in the categorical data, and the

**Table 1:** Demographic characteristics by existence of sleeping disorder

Variables		Non insomnia N=3,897 (%)		Insomnia N=840 (%)		p*
Gender	Male	952	87	146	13	<0.001
	Female	2,945	81	694	19	
Age	20-29	1,155	82	257	18	0.38
	30-39	1,129	84	222	16	
	40-49	941	82	201	18	
	over 50	672	81	160	19	
Occupation	Doctor	287	90	33	10	<0.001
	Nurse	2,389	80	616	20	
	Medical care personnel	586	88	83	12	
	Administrative staff	504	86	82	14	
	Skilled professionals	131	83	26	17	
Overtime work per month (hours)						
	under 20	2,648	83	549	17	0.006
	20-39	849	79	223	21	
	40-79	320	84	59	16	
	over 80	80	90	9	10	
Lifestyle related diseases						
	Hypertension	287	7	81	10	0.025
	Diabetes	85	2	24	3	0.236
	Metabolic Syndrome	308	8	95	11	0.001
	Low back pain	875	22	291	35	<0.001
	Headache	607	16	243	29	<0.001
Fatigue score, Mean, (SD)		6.2	(2.4)	7.4	(2.7)	<0.001
Depression score, Mean, (SD)		9.8	(3.9)	12.1	(4.9)	<0.001
Fatigue+Depression, Mean, (SD)		16.4	(5.4)	20.2	(6.5)	<0.001

SD; Standard deviation

\* All p values are for comparison of the characteristics of existence of insomnia and non-insomnia by analyses with the t-test or chi-square test.

t-test was used to compare the differences in the scores. The Shapiro-Wilk's normality test was also performed before the t-test. A P value of less than 0.05 was considered to indicate statistical significance. All analyses were performed using JMP10.0.0™ (SAS Institute Inc., NC, USA).

## 3 Results

### 3.1 Demographic characteristics

Of the 7,690 staff members who were given the questionnaire, 5,083 (66%) responded to the questionnaire. Of these 4,737 (62%) workers provided a completed questionnaire that was used in the analysis. Regarding the gender of the participants, 1,098 (23%) were male and 3,639 (77%) were female. Regarding the ages of the participants, 1,412 (30%) were in their 20's, 1,351 (29%) were in their 30's, 1,142 (24%) were in their 40's, and 832 (18%) were over 50. Regarding their occupation, 320 (7%) were doctors, 3,005 (63%) were nurses, 669 (14%) were medical care personnel, 586 (12%) were administrative staff, and 157 (3%) were skilled professionals. Regarding overtime work in the most recent month, 3,197 (67%) worked <20 hours, 1,072 (23%) worked 20–40 hours, 379 (8%) worked 40–80 hours, and 89 (2%) worked >80 hours. Regarding life-style related diseases, 368 (8%) were currently being treated or had received health guidance for hypertension, 109 (2%) for diabetes, 403 (9%) for metabolic syndrome, 1,166 (25%) for low back pain, and 850 (18%) for headaches (Table 1).

### 3.2 Sleep parameters

Among the participants, 840 (18%) suffered from some form of insomnia. Initial insomnia, middle insomnia, and terminal insomnia patterns overlapped in some individuals (i.e., have trouble both in getting to sleep and in waking up early in the morning). One hundred and forty-six (13%) men and 694 (19%) women suffered from insomnia. Among the nurses, 20% had insomnia, and that level was higher than that of the other occupations. Hypertension, metabolic syndrome, low back pain, and headaches were associated with insomnia. The average FS were 7.4 in chronic insomnia and 6.2 in non-insomnia. The average DS were 12.1 in chronic insomnia and 9.8 in non-insomnia. The average score for FS + DS were 20.2 in chronic depression and 16.4 in non-insomnia. All scores were significantly higher in participants with chronic

insomnia compared to that in those without chronic insomnia (Table 1).

### 3.3 Multiple regression analyses

Next, we performed a multiple logistic regression analysis on the data from the chronic insomnia group (IS>2) and the normal group. In the multiple logistic regression analyses, age over 50, nursing profession, low back pain, headaches, and depression score were significantly associated with the presence of chronic insomnia (Table. 2). We also used multiple regression models by gender setting the DS as an objective variable. The results are shown in Table 3. The regression models were controlled for age, occupation, overtime work, lifestyle-related diseases, chronic pain, insomnia, and fatigue. The male model's adjusted R square was 0.518, and the female's adjusted R square was 0.532. There were no interaction effects among the independent variables.

The variables that had significant negative impacts on the DS were males ages 30-39 (partial regression coefficient:  $b=0.357$ ,  $p=0.016$ ), females ages 20-29 ( $b=0.494$ ,  $p<0.001$ ), male administrative staff ( $b=0.475$ ,  $p=0.003$ ), males with metabolic syndrome ( $b=0.258$ ,  $p=0.023$ ), and for both genders chronic insomnia (male;  $b=0.480$ ,  $p<0.001$ ; female;  $b=0.485$ ,  $p<0.001$ ), and fatigue (male;  $b=1.180$ ,  $p<0.001$ ; female;  $b=1.151$ ,  $p<0.001$ ) (Table 3).

## 4 Discussion

Mental health assessments for workers should contain concrete measures to detect and to prevent both depression and other mental illnesses. Although there are several self-administered checklists on work stress, accumulated fatigue, and depression, a simple inclusive questionnaire is necessary. An amendment to the Industrial Safety and Health Law includes strengthening of mental health assessments by including a stress assessment in the medical health examinations for the purpose of detecting those suffering from a high level of stress. The nine items in the brief work stress questionnaire of anxiety, fatigue, and depression have become candidates for this assessment based on the reports by the National Institute of Occupational Safety and Health [13].

Chronic insomnia is the one of the factors influencing the development of mental illness. In this survey, we tried to clarify the relationship between chronic insomnia and various factors. Although there is no certainty about

**Table 2:** Logistic regression analysis regarding factors associated with chronic insomnia

Explanatory variable		Odds Ratio	
		(95%CI)	P
Gender	Male	1	
	Female	1.10(0.84-1.44)	0.472
Age (years)	20–29	1	
	30–39	0.96(0.78-1.18)	0.74
	40–49	1.07(0.86-1.33)	0.533
	Over 50	1.42(1.10-1.82)	0.005*
Occupation	Doctor	1	
	Nurse	1.60(1.03-2.55)	0.034*
	Medical care personnel	1.05(0.67-1.69)	0.81
	Administrative staff	1.23(0.79-1.97)	0.351
	Skilled professionals	1.50(0.82-2.70)	0.178
Overtime working (hours per month)	Under 20	1	
	20–39	1.09(0.90-1.31)	0.342
	40–79	0.90(0.65-1.23)	0.54
	Over 80	0.59(0.26-1.20)	0.155
Lifestyle-related disease	Hypertension	1.25(0.92-1.69)	0.146
	Diabetes	0.80(0.46-1.34)	0.417
	Metabolic syndrome	1.29(0.97-1.69)	0.072
	Lower back pain	1.33(1.11-1.58)	0.001*
	Headache	1.66(1.37-2.00)	<0.001*
Fatigue score		1.02(0.93-1.15)	0.384
Depression score		1.10(1.05-1.18)	<0.001*

CI: Confidence Interval

\*p&lt;0.05

This model's evaluation: Likelihood-ratio test: p&lt;0.001, Nagaike R square=0.104, AICc=4157.4

The model adjusted for gender, age group, Occupation, Overtime working hours per month, Lifestyle-related diseases such as Hypertension, Diabetes, Metabolic Syndrome, Lower back pain, Headache, fatigue score, and Depression score

other possible independent variables, multiple regression analyses suggested that chronic insomnia is an important factor for depression. Koyama et al. found that subjects who suffered from severe sleeping disorders, not just during depression, tended to have decreased blood flow in the frontal lobe of the brain [2]. When SIGH-D was used to evaluate sleeping disorders, an IS of 3 or higher showed that its severity and the reduced blood flow in the frontal lobe are significantly correlated. Based on this biological finding, preliminary research was conducted with 108 working participants, which included healthy participants and patients with mild to moderate depressive episodes. The result showed that the IS was significantly correlated with the severity of depression, subjective fatigue,

sadness, and suicidal thoughts. Thus, an IS evaluation has the possibility of identifying depression based on a questionnaire survey related to direct mood changes [3].

There have been robust findings concerning the biology underlying the close relationship between sleep disorders and depression. For example, Buckley has found that a protracted sleep disorder, not depression, induces hyperactivity of the HPA (hypothalamic-pituitary-adrenal axis) system [14]. Furthermore, exposure to extreme stress causes the excessive secretion of corticotropin releasing hormone (CRH) —a cerebral mechanism for stress adaptation. This release of CRH inhibits the activities of the serotonin pathway in the nervous system that extends from the dorsal raphe nucleus to the prefrontal area via the

**Table 3:** Multiple regression analysis by gender with depression criterion variable

Explanatory variable		Male (N = 1,098)		Female (N = 3,639)	
		b	P	b	P
Age (years)	20–29	-0.114	0.543	0.494	<0.001*
	30–39	0.357	0.016*	-0.281	<0.001*
	40–49	-0.073	0.619	-0.243	<0.001*
	Over 50	-0.169	0.291	0.029	0.785
Occupation	Doctor	-0.331	0.08	-0.007	0.982
	Nurse	0.103	0.673	0.21	0.088
	Medical care personnel	-0.084	0.589	0.219	0.188
	Administrative staff	0.475	0.003*	-0.011	0.946
	Skilled professionals	-0.164	0.542	-0.41	0.14
Overtime working (hours per month)	Under 20	0.09	0.588	-0.126	0.431
	20–39	0.26	0.115	-0.04	0.811
	40–79	-0.27	0.153	0.114	0.582
	Over 80	-0.08	0.784	0.053	0.901
Lifestyle-related disease	Hypertension	0.193	0.096	-0.234	0.058
	Diabetes	-0.07	0.717	0.399	0.075
	Metabolic syndrome	0.258	0.023*	0.064	0.562
	Lower back pain	-0.129	0.222	0.024	0.675
	Headache	0.045	0.765	0.026	0.666
Insomnia	Yes	0.48	<0.001*	0.485	<0.001*
Fatigue score		1.18	<0.001*	1.151	<0.001*

\*p&lt;0.05

Adjusted R square; Male:0.518, Female:0.532

gamma-aminobutyric acid (GABA) system [15]. It is also known that CRH has a stimulant effect [14]. Therefore, it is inferred that a substantive lack of sleep will lead to a sustained activation of the HPA system once again, thus establishing a vicious cycle.

On the other hand, the decline in frontal lobe function due to depression has been established by several earlier studies, including those that used functional brain imaging [15–18]. The protraction of a sleep disorder activating the HPA system and inhibiting the serotonin nervous system in the frontal lobe is believed to elicit a clinical condition similar to depression. Furthermore, the finding that the hyperactivity of the HPA system increases cortisol secretion, which inhibits the HPA system and damages hippocampal cells, further strengthens the suggested relationship between sleep disorders and depression. This biological finding strengthens the theory that a lack of sleep due to insomnia, exposure to stress, and over-

work, leads to depression because of the accumulation of mental fatigue.

Insomnia has been found among 80–85% of individuals with depression, and there have even been reports that depression manifests prior to the core symptoms, such as depressed moods [19]. In other words, the view that lack of sleep due to its chronicity initiates depression in advance [20,21] is supported by longitudinal epidemiological studies, such as those by Chang *et al.* and Riemann & Voderholzer both of which showed that participants with a history of insomnia are significantly more likely to suffer from depression later in their lives [22,23]. In light of the above findings and this study's results, it is noteworthy that the IS, which showed a correlation with biological decline in frontal lobe functions, was also correlated with depression symptoms. Thus, the IS is considered to be an effective interview item in future studies on workers' pre-

ventative medical care for the early identification of those likely to suffer from depression.

There are also relationships between lifestyle-related diseases and chronic insomnia. There have been many reports that a sleep disorder is related to the induction and exacerbation of lifestyle-related illnesses [24,25]. According to Uchimura, those who suffer from lifestyle-related diseases are significantly more likely to experience insomnia [26]. In the present study, hypertension, diabetes, and metabolic syndrome were not associated with chronic insomnia. The most likely reason for the lack of association of these diseases with chronic insomnia is due to the limited number of the patients with these diseases in the study. Only 109 people with diabetes were present in the total of 4,737 people (2.3%). In addition, patients with hypertension only numbered 368 (7.8%), and those with metabolic syndrome only numbered 403 (8.5%). These numbers represent a much lower prevalence than that in the normal population [27,28]. In the present study, our enrolled subjects were health-related workers, so they tend to pay more attention to prevent these diseases than other types of workers. We conclude that our patient number was too small, especially with the insomnia cases, to identify a relationship between these diseases and chronic insomnia.

However, the relationships between chronic insomnia and chronic pain (e.g., headaches and lower back pain) were identified as being associated with insomnia in this survey. Those suffering from headaches had a significantly higher tendency to suffer from insomnia. Since mobility tension and muscle tonus are heightened in association with the stimulation of the sympathetic nervous system [29], it is easy to understand the correlation between insomnia and chronic headaches. Furthermore, it is known that the descending inhibitory systems that function against pain decrease during a depressed state, thus decreasing the pain threshold [30].

Conventionally, there is a category for somatoform pain disorder in the assessment of psychiatric patients, indicating that the correlation between depression and complaints of pain has been established. Labbé et al. reported a correlation of work fatigue and hours with the severity of headaches in a cohort study conducted with factory employees [31].

Most of the lower back pain reported is generally non-specific chronic lower back pain. In this study, participants who suffered from lower back pain had a significantly higher degree of insomnia. Recently, researchers have not been in agreement about the correlation between chronic lower back pain and psychosocial factors and fear avoidance [32,33]. However, in light of the above-men-

tioned decline in the descending inhibitory system function and the concept of a somatoform disorder, the correlation with depression is conventionally thought to be more valid.

There are several limitations in our study. First, our findings can only show association rather than causation because the study design was cross-sectional. Second, as the data were self-reported, we cannot fully rule out reporting errors. Third, the response rate of the current study was moderately satisfactory (66%). Since the hospital workers who did not respond to our questionnaire survey might have been those who were busier and had higher occupational stress, there might have been selection bias, which, if any, might have led to conservative estimates of the prevalence of occupational stress, such as depression, fatigue, and insomnia. Finally, this study was conducted only in 10 Rosai hospitals in Japan. Although 10 Rosai hospitals are located all over the Japan, but not in the central area, the findings of this study cannot be generalized to other hospital workers without caution.

Despite these limitations, it could be said that the IS (insomnia score), which served as the starting point for this research study, is a predictive factor for the detection of early depression. Determining insomnia as a risk factor for depression as well as a high level of stress and lifestyle-related diseases is a significant observation that can open the door to preventative care for a wide spectrum of disorders. Specifically, the IS, the nine items on depression and fatigue, and the existence of lifestyle-related diseases and chronic pain should be confirmed during a medical examination interview, which could enable early identification of the risks of illnesses caused by this mental health disorder. Learning from the results of this study and utilizing the size of our Japan Labor Health and Welfare Organization, we intend to use the IS in preventative medical care and in industrial healthcare settings.

**Acknowledgements:** This research is a part of the research, development, and dissemination projects related to the 13 fields of occupational injuries and illnesses of the Japan Labor Health and Welfare Organization.

**Conflict of interest statement:** Authors state no conflict of interest

## References

- [1] Koyama F., Changes in regional cerebral blood flow correlate with severity of depression and the feeling of fatigue, a

- 99mTc-ECD SPECT Study in 45 Workers, *Job Stress Research*, 2010, 17, 133–137 (in Japanese)
- [2] Koyama F., Matsuura N., Kageyama J., Otsuki K., Changes in regional cerebral blood flow correlate with symptoms of depression, severity of fatigue, and sleep disorders in 99mTc-ECD SPECT study in 45 workers, *Jpn J Occup Med Traumatol.*, 2010, 58, 76–82 (in Japanese)
- [3] Koyama F., Kubuki Y., Uragami I., For early detection of “potential patients with depression”- Correlation of sleep disorder with frontal lobe dysfunction and depression symptoms, *Jpn J Occup Med Traumatol.*, 2011, 59, 32–39 (in Japanese)
- [4] Williams J.B., A structured interview guide for the Hamilton Depression Rating Scale. *Arch Gen Psychiatry.*, 1988, 45(8), 742–747
- [5] de Castro, A. B., Fujishiro, K., Rue, T., Tagalog, E. A., Samaco-Paquiz, L. P. G., Gee, G. C., Associations between work schedule characteristics and occupational injury and illness, *Int Nurs Rev.*, 2010, 57(2), 188–194
- [6] Ito S., Fujita S., Seto K., Kitazawa T., Matsumoto K., Hasegawa T., Occupational stress among healthcare workers in Japan, *Work.*, 2014, 49(2), 225–234
- [7] Caruso, C. C., Negative impacts of shiftwork and long work hours, *Rehab Nurs*, 2014, 39, 16–25
- [8] Nakane Y, Williams JBW., HAM-D Kozoka Mensetsu SIGH-D, 2004, Seiwa Shoten Co., Ltd., Tokyo (in Japanese)
- [9] Saito S, Takahashi N, Ishihara R, Ikeda M, Suzuki T, Kitajima T., et al., Association study between vesicle-associated membrane protein 2 gene polymorphisms and fluvoxamine response in Japanese major depressive patients, *Neuropsychobiology*, 2006, 54(4), 226–230
- [10] Kishi T, Kitajima T, Ikeda M, Yamanouchi Y, Kinoshita Y, Kawashima K, et al., CLOCK may predict the response to fluvoxamine treatment in Japanese major depressive disorder patients, *Neuromolecular Med*, 2009, 11(2), 53–57
- [11] Okuda A, Kishi T, Okochi T, Ikeda M, Kitajima T, Tsunoka T., et al., Translin-associated factor X gene (TSNAX) may be associated with female major depressive disorder in the Japanese population, *Neuromolecular Med*, 2010, 12(1), 78–85
- [12] Inoue A., Kawakami N., Shimomitsu T., Tsutsumi A., Haratani T., Yoshikawa T., et al., Development of a short version of the new brief job stress questionnaire, *Ind Health.*, 2014, 52, 535–540
- [13] Kawakami N., Improvement of work environment, *Sangyo Eiseigaku Zasshi*, 2002, 44, 95–99 (in Japanese),
- [14] Buckley T.M., Schatzberg A.F., On the interactions of the hypothalamic-pituitary-adrenal (HPA) axis and sleep, normal HPA axis activity and circadian rhythm, exemplary sleep disorders, *J Clin Endocrinol Metab.*, 2005, 90, 3106–3114
- [15] Ruggiero D.A., Underwood M.D., Rice P.M., Mann J.J., Arango V., Corticotrophic-releasing hormone and serotonin interaction in the human brainstem: behavioral implications, *Neuroscience*, 2000, 91, 1343–1354
- [16] Drevets W.C., Neuroimaging studies of mood disorders, *Biol Psychiatry*, 2000, 48, 813–829
- [17] Smith D.J., Cavanagh J.T., The use of single photon emission computed tomography in depressive disorders, *Nuclear Medicine Communications*, 2005, 26, 197–203
- [18] Okada G., Okamoto Y., Morinobu S., Yamawaki S., Yokota N., Attenuated left prefrontal activation during a verbal fluency task in patients with depression, *Neuropsychobiology*, 2003, 47, 21–26
- [19] Kaneita Y., Ohida T., Uchiyama M., Takemura S., Kawahara K., Yokoyama E., et al., The relationship between depression and sleep disturbances: A Japanese nationwide general population survey, *J Clin Psychiatry*, 2006, 67, 196–203
- [20] Shimizu T., Modern society and sleep. In order to have a good sleep. Sleep disorder. Depression and sleep disorder, *Clinical Practice*, 2005, 24, 833–836 (in Japanese)
- [21] Ohayon M.M., Roth T., Place of chronic insomnia in the course of depressive and anxiety disorders, *J Psychiatr Res*, 2003, 37, 9–15
- [22] Chang P.P., Ford D.E., Mead L.A., Cooper-Patrick L., Klag M.J., Insomnia in young men and subsequent depression. The Johns Hopkins Precursors Study, *Am J Epidemiol*, 1997, 146, 105–114
- [23] Riemann D., Voderholzer U., Primary insomnia; a risk factor to develop depression? *J Psychiatr Res*, 2003, 76, 255–259
- [24] Gottlieb D.J., Punjabi N.M., Newman A.B., Resnick H.E., Redline S., Baldwin C.M., et al., Association of sleep time with diabetes mellitus and impaired glucose tolerance, *Arch Intern Med*, 2005, 165, 863–867
- [25] Spiegel K., Leproult R., Van Cauter E., Impact of sleep debt on metabolic and endocrine function, *Lancet*, 1999, 354, 1435–1439
- [26] Uchimura N., Relationship between sleep disorders and lifestyle-related disease (Symposium : Psychosomatic Function and Sleep Disorders), *Jpn J Psychosom Med*, 2007, 47, 771–776 (in Japanese)
- [27] Yamagishi K., Iso H., The criteria for metabolic syndrome and the national health screening and education system in Japan, *Epidemiol Health*, 2017, 39, e2017003
- [28] Ikeda N., Inoue M., Iso H., Ikeda S., Satoh T., Noda M., et al., Adult mortality attributable to preventable risk factors for non-communicable diseases and injuries in Japan: a comparative risk assessment, *Plos med*, 2012, 9(1), e1001160
- [29] Ogawa Y., Kanbayashi T., Saito Y., Takahashi Y., Kitajima T., Takahashi K., et al., Total sleep deprivation elevates blood pressure through arterial baroreflex resetting: A study with microneurographic technique, *Sleep*, 2003, 26, 986–989
- [30] Basbaum A.I., Fields H.L., The origin of descending pathways in the dorsolateral funiculus of the spinal cord of the cat and rat: further studies on the anatomy of pain modulation, *J Comp Neurol*, 1979, 187, 513–531
- [31] Labbé E.E., Murphy L., O'Brien C., Psychosocial factors and prediction of headaches in college adults, *Headache*, 1997, 37, 1–5
- [32] Geisser M.E., Haig A.J., Wallbom A.S., Wiggert E.A., Pain-related fear, lumbar flexion, and dynamic EMG among persons with chronic musculoskeletal low lower back pain, *Clin J Pain*, 2004, 20, 61–69
- [33] Leeuw M., Goossens M.E., Linton S.J., Crombez G., Boersma K., Vlaeyen J.W., The fear-avoidance model of musculoskeletal pain: current state of scientific evidence, *J Behav Med*, 2007, 30, 77–94